REMARKS

The issues outstanding in the Office Action of May 26, 2009, are the claim objections, and rejections under 35 U.S.C. 101 and 112. Reconsideration of these issues, in view of the following discussion, is respectfully requested.

Claim Objections

Claim 6 has been objected to because of a typographical error. This claim has been amended, and withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. 101

Claims 13 and 15 have been rejected under 35 U.S.C. 101, as they recite a "use" in non-standard, U.S. format. Reconsideration of this rejection is respectfully requested, in view of the reformatting of the claims for U.S. practice. It is respectfully submitted that this reformatting does not change the scope of these claims, either literally or for purposes of the doctrine of equivalents. Withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. 112

Claims 13 and 15 have been rejected under 35 U.S.C. 112, for the reasons set forth in the rejection under 35 U.S.C. 101. In view of the foregoing discussion, withdrawal of this rejection is also respectfully requested.

Claims 1-15 have been rejected under 35 U.S.C. 112, first paragraph. Reconsideration of this rejection is also respectfully requested.

At page 3 of the Office Action, it is argued that "derivatives" and "solvates" of compounds of the invention are not enabled, although the Office Action admits, however, that salts and stereoisomers of compounds of formula I are, in fact, enabled by the specification. While Applicants do not agree that at least solvates are non-enabled, inasmuch as the production of solvates is highly conventional in the art, in order to expedite prosecution and for business reasons the derivatives and solvates have been canceled from the present claims. Withdrawal of

this rejection is accordingly respectfully requested.

Claims 13 and 15 have been rejected under 35 U.S.C. 112, first paragraph. Reconsideration of this rejection is also respectfully requested. It is argued, at page 6 of the Office Action, that "the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided." This rejection is not fully understood, inasmuch as claims 13 and 15 recite a variety of indications which are clearly defined, and well understood by one of ordinary skill in the art. The fact that some terms may encompass later discovered diseases is not seen, in and of itself, to be fatal to enablement, inasmuch as the specification clearly enables one of ordinary skill in the art to treat any such disease, in the same manner in which the disease is listed in the claims are treated.

Moreover, it appears that the real concern of the Office Action in the passages at pages 6-12 of the Office Action appears to be the breadth of the claims. As such, this concern is not seen to be relevant to enablement of the claims.

First, at page 2, lines 10 - 17, it is taught that the compounds of formula I inhibit factor Xa, VIIa and IXa, and this statement is supported at page 3, lines 21-22 and page 3, lines 30 – page 4, line 26, with a discussion of the methods used to determine this activity in the subject compounds. At this portion of the specification, it is taught that the compounds thus are useful to treat thromboembolic diseases, such as thrombosis, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty and claudicatio intermittens. At page 4, lines 29 – 35 and page 5, lines 1-7, it is taught that factor VIIa inhibitors also inhibit the growth of tumor cells and may furthermore be used for tumor therapy. Clearly, this discussion, *without more*, is sufficient to establish utility of the application for purposes of §112 of the statute, as it constitutes a scientifically supportable statement of utility which would be plausible to one of ordinary skill in the art.

It is well established that an unsupported suggestion that reactants within a class defined by claims in a typical method of use application would not work, or that such claims embrace inoperative members, insufficient basis alone for rejecting the claims. See *Ex parte Janin*, 209 U.S.P.Q. 761 (POBA 1979). In fact, it is clear that recitations in an Applicant's specification *must* be taken by the PTO as an assertion that all compounds encompassed in the claims are operative in

the invention, in the absence of reasons or evidence to the contrary. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971).

The first paragraph of 35 U.S.C §112 requires only *objective* enablement. Where a specification teaches the manner and process of making and using the invention, the specification *must* be taken as sufficient under §112, unless there is reason to doubt the truth of these statements. See *Marzocchi*, supra. Applicants' specification clearly enables one to make and use the disclosed compounds in the claimed methods, as evidenced from the disclosure at page 5 - 7 setting forth pharmaceutical formulations and dosages and the examples which also detail the production of a pharmaceutical formulations.

On the one hand, it is submitted that the Examiner has not provided any such reasons or evidence to doubt the assertion of utility in the specification and, thus, the further steps of the analysis as set forth in *Marzocchi* are not reached. As clearly stated in *Marzocchi*, mere *breadth* of the claims does not, without more, result in non-enablement. As the court stated,

> Turning specifically to the objections noted by the Board as indicated above, it appears that these comments indicate nothing more than a concern over the *breadth* of the disputed term. If we are correct, then the relevance of this concern escapes us. It has never been contended that Applicants, when they included the disputed terms in their specification, intended only to indicate a single compound. Accepting, therefore, that the term is a generic one, its recitation must be taken as an assertion by Applicants that all of the 'considerable number of compounds' which are included in the generic term would, as a class, be operative to produce the asserted enhancement of adhesion characteristics. The only relevant concern of the patent office under these circumstances should be over the *truth* of any such assertion. The first paragraph of §112 requires nothing more than *objective enablement*. How such a teaching is set forth, either by the use of illustrative examples or by broad term analogy, it is of no importance.

Marzocchi, supra. Emphasis in original. Thus, the concern expressed at pages 6 and 7 of the Office Action, apparently that the term tumor used in the claimed methods is broad, does not provide the

reasons or evidence necessary by *Marzocchi* to pass beyond the necessity for objective enablement.

Further, in this regard, it is important to note, as a matter of law, that it is not necessary for Applicants' *method* claims to exclude inoperative embodiments, inasmuch as the claims are interpreted in light of the level of understanding one of ordinary skill in the art and, for methods, are interpreted to be *per se* functional. See *In re Angstadt*, 190 U.S.P.Q. 214 (CCPA 1976) and *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (CCPA 1974). These cases state that, for method claims, inoperative embodiments are not encompassed therein and the only question is whether it would be undue experimentation for one of ordinary skill in the art to determine the scope of the claim. This issue is discussed more fully below. Moreover, anti-tumor utilities are no longer to be considered to be "special", i.e., per se incredulous, by the Patent and Trademark Office. See *Ex parte Rubin*, 5 U.S.P.Q. 2d 1461 (BPAI 1987). As such, applications claiming these methods are, therefore, no more than typical method of use applications wherein the existence of reliable screening protocols correlatable with pharmaceutical activity in humans is sufficient to satisfy §112, in the absence of reasons to the contrary. As noted above, screening protocols for determining the efficacy of the compounds in the anti-tumor utilities are set forth in the specification where it is indicated that the details of using a given compound can be determined by routine testing using a known protocol which is correlated with human activity, again, see page 4, lines 4 - 15 and 29 - 35.

Thus, the only way that the issue of "undue experimentation" come up is if the PTO were to furnish reasons or evidence why the objective enablement of the present specification fails (none have been advanced) or it is alleged it would have been undue experimentation to determine the *scope* of the present method claims. This allegation has not been advanced. Thus, the discussion of *In re Wands*, taking up a substantial amount of the Office Action, does *not* provide the necessary reasons or evidence as to why utility is deficient, but instead is reached only in other circumstances. However, since this analysis has been given considerable breadth in the Office Action, it will be addressed herein.

With respect to the nature of the invention, the fact that other treatable tumors may later be discovered is not relevant to enablement, which is judged at the time of filing.

With respect to the state of the art and predictability, *absolute* predictability has never been required. It is important to note that a determination of undue experimentation must be considered

on a *compound by compound* basis. The mere fact that a claim is broad does *not* mean that it is undue experimentation is required to determine enablement of the compounds therein, if it is not undue experimentation to determine enablement for *each* compound in the scope of the claim. See, for example, *In re Colianni*, 195 U.S.P.Q. 150 (CCPA 1977). One of ordinary skill in the art can easily determine, with the protocols given in the specification, whether a given compound has the utility stated. Thus, the mere fact that many compounds must be tested is not dispositive of lack of utility.

With respect to the guidance given by the instant specification, is submitted that the guidance is adequate, inasmuch as pharmaceutical formulation information is given, one of ordinary skill in the art can clearly prepare the compounds for administration, dosages are given and the pharmaceutical art is well developed and administration of a compound for a given indication is quite routine.

Pharmacological data is given at page 21, where test results prove inhibiting activity on factor Xa and TF/FVIIa. The discussion at pages 7 and 8 of the Office Action appears to be speculation on the part of the PTO that mechanisms are not well understood; however, elucidation of a mechanism is *not* necessary, where sufficient instruction is given to administer the compounds to produce the desired effect. Thus, it is submitted that this is also a non-issue.

With respect to working examples, it is well established that working examples are *not* required to provide enablement. See, for example, *In re Borkowski*, cite.

With respect to the state of the art, the noted inhibitors are well known to be implicated in signaling pathways which are instrumental in the formation of tumors. Thus, it is again not seen that this is an issue. With respect to the quantity of invention necessary, this has been discussed above. It is maintained that the fact that a claim may be broad does not, in and of itself, result in undue experimentation, if the testing of, for example, each type of tumor is routine. Thus, this is not seen to be basis for lack of enablement.

In conclusion, it is submitted that the wands factors clearly do not result in undue experimentation in order to determine whether a given cancer and/or autoimmune disease and/or a compound is within the scope of the present claims. Thus, objective enablement is clearly present, and withdrawal of the rejection under 35 U.S.C §112 is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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